Electrophilic 1,3-C→N⁻ and -N→C⁻ migrations in saturated systems

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A new type of intramolecular electrophilic rearrangements involving the shift of COOAlk groups from carbon to an N-anionic center is considered. Carbanionic species with COOAlk groups at anionic centers containing no acidic hydrogen react unusually with alkyl(aryl) iso(thio)cyanates giving carbamates as a result of insertion of RNCX into the C—C bond. The kinetics and mechanism of insertion of aryl isocyanates into the C—C bond of the phosphonium zwitterion obtained from triisopropylphosphine and ethyl 2-cyanoacrylate are discussed. The reaction of α-carbanions derived from *N,N*-disubstituted amides with methyl trifluoromethanesulfonate result in *O*-methylation. Some possibilities of back N→C⁻ migrations are considered.

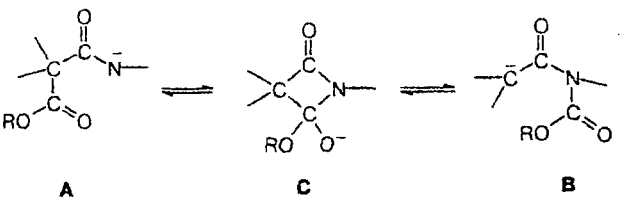
Key words: phosphonium zwitterions, alkyl(aryl) iso(thio)cyanates, carbanions, electrophilic rearrangements, insertion reactions, carbamates, α-carbanions of *N,N*-disubstituted amides, methyl trifluoromethanesulfonate, X-ray diffraction analysis.

Intramolecular electrophilic rearrangements in saturated systems consisting in the migration of electron-deficient groups to anionic centers have been reported. Thus the Smiles rearrangement is migration of aryl groups between the anionic centers formed by oxygen, sulfur, or nitrogen atoms[1]; Stevens has described migration of alkyl cations from positively charged nitrogen, phosphorus, sulfur, antimony, or arsenic atoms to a carbanionic center[2]; a shift of alkyl groups from oxygen to a carbanionic center was discovered by Wittig.[3] Processes with close chemical natures have been reported by Wawzonek,[4] Truce,[5] Grovenstein,[6] Zimmerman,[7] and Luttringhaus.[8] In some cases, with a particular environment of the reaction centers, reversible migration of cationic species can occur.[9] Since, according to their chemical essence, these processes can be classified as nucleophilic substitution induced by an attacking anion, we expected that new intramolecular migrations including those accompanied by rupture or formation of C—C bonds could be found.

As a working scheme (with allowance for the general principles of the molecular design of tautomeric systems[9]), we have chosen intramolecular transformations of a previously unknown type, namely those due to 1,3-migrations of electron-deficient species between C- and N-anions in saturated structures **A** and **B** (Scheme 1).

Structures **A** and **B** were chosen due to the necessity of observing known[9] electronic and steric conditions needed for maintenance of the contact between the key atom of the migrating group and the site to which this group migrates to give transition state **C**. The structure

Scheme 1



A **C** **B**

of species **A** and **B** should also ensure delocalization of electrons in transition state **C**, which would create conditions for the rupture of the previous bond and for the formation of the new one. The geometric parameters of substituted amides **A** and **B** allow one to count on an effective intramolecular contact of the N-anion **A** with the key atom of the migrating substituent and, correspondingly, of the C-anion **B** with the same key atom. Presumably, migration of a group from carbon to nitrogen or back would be determined by the electronic structure, configuration, and the size of substituents at the C- and N-anionic centers.

A convenient method for the preparation of *N*-monosubstituted carboxamides by the reaction of carbanions with iso(thio)cyanates has long been known.[10] The first step in this transformation (for example, that involving carbanions based on alkyl cyanoacetate, Scheme 2) gives N-anions **1**, which undergo intramolecular protonation and are isolated after acidification as *N*-monosubstituted amides **2**.

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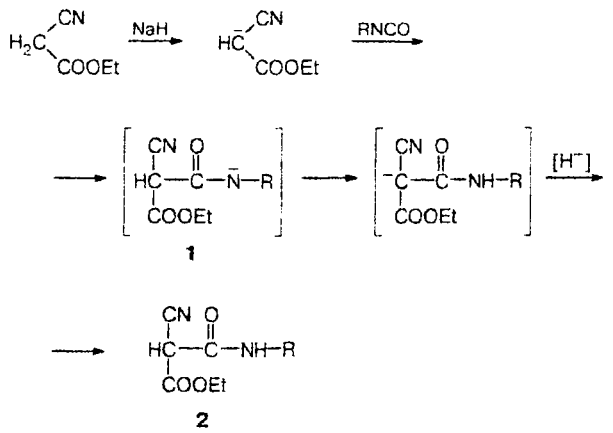
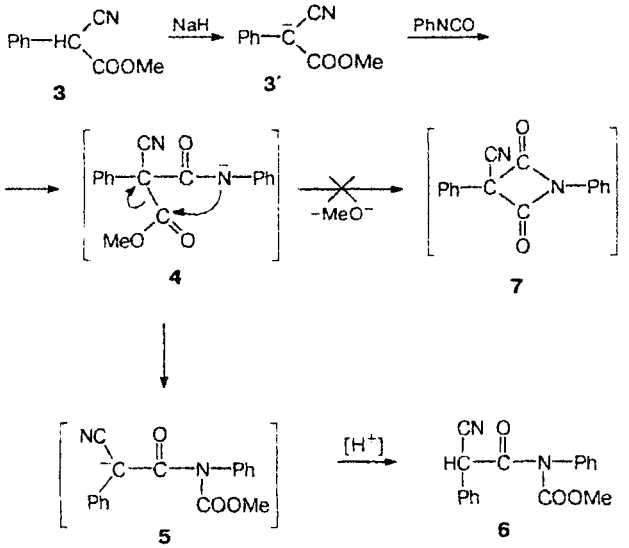
Scheme 2



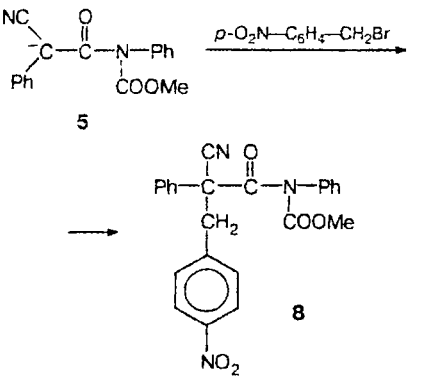
We expected that, when esters **3** of substituted carboxylic acids, which have only one active hydrogen atom, are introduced into this type of reaction, the anionic center of the N-anion **4** arising initially can attack the carbon atom of the carboxylate group with migration of the latter to the nitrogen atom to give carbanion **5** and, after acidification, carbamate **6**. Naturally, we have also considered the possibility of elimination of only the alkoxide anion upon this attack. This reaction route is, in principle, possible but, since the four-membered ring in **7** remains highly strained (Scheme 3),[11] it seems relatively unlikely.

Scheme 3



In fact, the reaction of phenyl isocyanate with carbanion **3'** gives carbamate **6**, whose structure follows from its physicochemical characteristics[12] and chemical properties. In particular, the intermediate carbanion **5** reacts with *p*-nitrobenzyl bromide to give *C*-alkylation product **8** in a low yield (Scheme 4).

Scheme 4

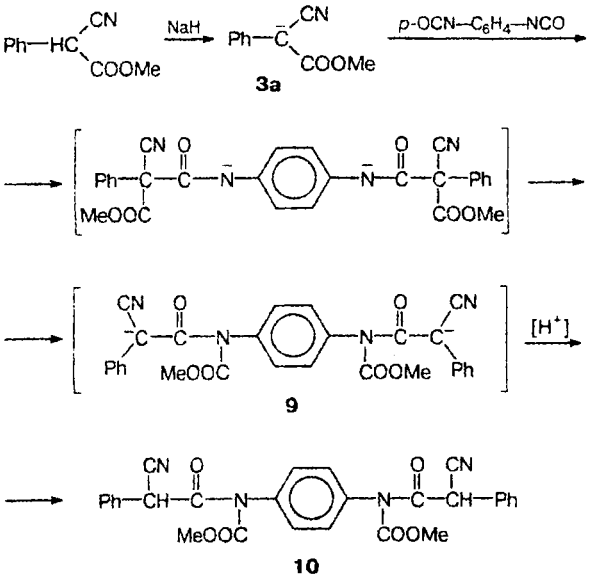


The reactions of carbanion **3a** with *p*-phenylene diisocyanate (Scheme 5) and other related bis(isocyanates) occur equally smoothly. This yields bis-carbanions of type **9**, which are promising starting compounds for organic and polymer chemistry.

The reactions depicted in Schemes 3 and 5 occur over 1—2 h; the yields of the rearrangement products reach 60—80%. The transformations shown in Schemes 3 and 5 can formally be regarded as insertion of isocyanates into the C—C bond. Such transformations of isocyanates have not been reported previously.

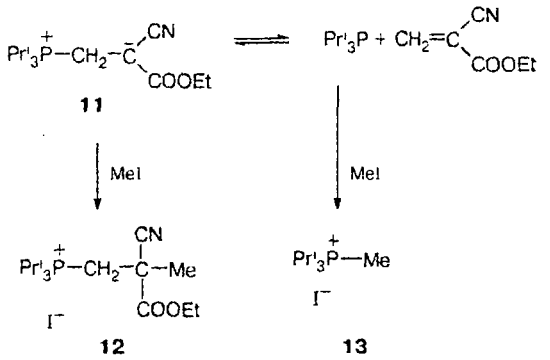
The reaction of iso(thio)cyanates with carbanions **11**, containing a phosphonium group, proved to be a

Scheme 5



convenient model for investigation of the C→N migrations of the alkoxycarbonyl groups in question. Zwitterions of type **11** are easily formed under strictly definite conditions upon the reaction of 2-cyanoacrylates with trialkylphosphines (or with hexaethyltriaminophosphine to prepare the corresponding triamides).[13,14] According to the data of ^{31}P NMR spectroscopy, a solution in CH_2Cl_2 contains only zwitterion **11**; however, in THF, apart from carbanion **11**, triisopropylphosphine is also detected spectroscopically (δP +20.67). The same signal appears when triethylamine is added to a solution of zwitterion **11** in dichloromethane. Thus, N-donor solvents induce dissociation of zwitterion **11** to give initial reactants. The equilibrium is additionally shifted to the right due to the rapid polymerization of the ethyl 2-cyanoacrylate formed. It is of interest that in dichloromethane in the presence of a large excess of methyl iodide, zwitterion **11** is converted into two phosphonium salts. One salt (**12**) results from methylation of zwitterion **11**, and the other one (**13**) is the phosphonium salt derived from triisopropylphosphine and methyl iodide (Scheme 6).

Scheme 6

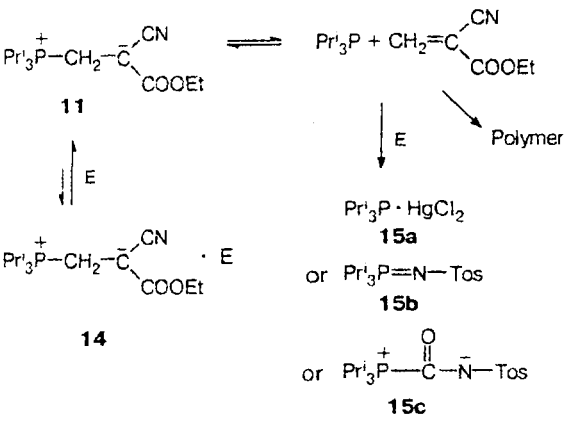


Apparently, dissociation of zwitterion **11** to give triisopropylphosphine occurs as well in dichloromethane in the presence of a large excess of MeI. When equimolar amounts of the reactants are used, the corresponding *C*-alkylated products of type **12** are produced in high yields.[15]

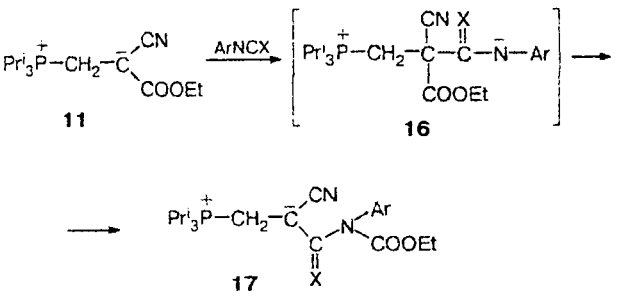
The data presented above can be used for an attempt to explain the outcome of the reaction of zwitterion **11** with highly reactive electrophiles (E), tosyl azide, tosyl isocyanate,[16] and mercury(II) dichloride. Zwitterion **11** reacts with these three compounds in dichloromethane extremely rapidly. The three reactions yield the corresponding trialkylphosphine and the polymer of ethyl 2-cyanoacrylate. Since the formation of adducts **14** formed by zwitterion **11** and these reagents is obviously reversible, triisopropylphosphine derivatives are formed as the final stable products **15** (Scheme 7).

A different situation is observed when zwitterion **11** and its analogs react with alkyl or aryl iso(thio)cyanates.[16–22] In these cases, the primary addition product **16** rapidly isomerizes to carbamate **17** (Scheme 8). Thus, a rearrangement occurs similar to that observed for carbanions **3'**.

Scheme 7



Scheme 8



Ar = Ph, 1-naphthyl, *m*-MeC_6H_4, *p*-ClC_6H_4, *m*,*p*-$Cl_2C_6H_3$, *p*-$O_2NC_6H_4$; X = O, S

The transformations of the initial zwitterion **11** into carbamates **17** can be conveniently monitored by ^{31}P NMR spectroscopy, because the difference between the chemical shifts of the initial zwitterion **11** and carbamates **17** can reach several ppm. However, the formation of intermediate adducts **16** cannot be detected by this method. The structure of the products of this rearrangement was proved by X-ray diffraction analysis[16,18,20]; especially important results were obtained in the X-ray diffraction study of the product obtained by the reaction of zwitterion **11** with phenyl isothiocyanate, because they proved rigorously the presence of the phenyl isothiocyanate fragment between the C—C bonds of the initial zwitterion **11**.

A kinetic study fulfilled by the spectrophotometric method at Kazan University demonstrated that the reaction has the overall second order and the first order with

Table 1. Rate constants (k_2) and spectral (λ) and activation ($\Delta H^{\neq}$ and $\Delta S^{\neq}$) parameters for the reaction of zwitterion **11** with aryl isocyanates ArNCO (MeCN, 30 °C)

Ar	λ/nm	k_2/L mol^{-1} min^{-1}	$\Delta H^{\neq}$/kcal mol^{-1}	$-\Delta S^{\neq}$/eu	σ*
Ph	300	0.030	9.58	41.5	0.64
1-Naphthyl	330	0.034	9.15	42.2	0.70
p-$MeOC_6H_4$	305	0.095	8.58	43.1	0.74
m,p-$Cl_2C_6H_3$	305	0.488	7.15	44.54	1.10
o-$O_2NC_6H_4$	370	37.73	2.66	50.72	1.88

respect to each reactant.[23] The rate constants and activation parameters found in this study are presented in Table 1.

The excellent linear correlation between the activation enthalpy and entropy (Eq. (1), ΔH is expressed in cal mol^{-1}) indicates that all of the studied reactions belong to the same reaction series:

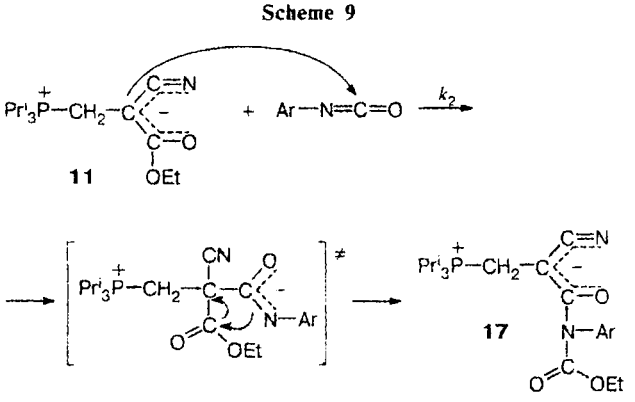
$$\Delta H^{\neq} = (41156\pm2800) + (759.5\pm62)\Delta S^{\neq}, \quad (1)$$

$$r = 0.999.$$

The isokinetic temperature found from this correlation is equal to 759.5±62 K, which is much higher than the experimental temperature range; therefore, the reaction is subject to clear-cut entropy control, *i.e.*, its rate sharply increases as the activation enthalpy decreases (see Table 1).

The kinetic data obtained and, in particular, the great negative value of the activation entropy points to a high degree of ordering in the activated complex, typical of cyclic structures. In all probability, the nucleophilic attack by the anionic center of zwitterion **11** on the carbon atom of the isocyanate group and the nucleophilic attack of the nitrogen atom on the ethoxycarbonyl group, resulting in the rupture of the C—C bond, occur roughly synchronously within one transition state according to a concerted mechanism (Scheme 9).

Scheme 9



Apparently, the driving force of the migration of the ethoxycarbonyl group to the nitrogen atom is the energy benefit due to the more efficient delocalization of the negative charge in the resulting compound **17**. More evidence supporting this mechanism is the influence of substituents in the aromatic ring of aryl isocyanate. These data are consistent with the fact that the nucleophilic attack by zwitterion **11** on the carbon atom of the isocyanate group is the rate-determining step of the reaction. The negative charge on the nitrogen atom thus arising accounts for the observed high sensitivity of the reaction rate to the influence of substituents. The logarithms of the rate constants obey an excellent correlation with the Taft inductive σ* constants of aromatic substituents at the nitrogen atom:

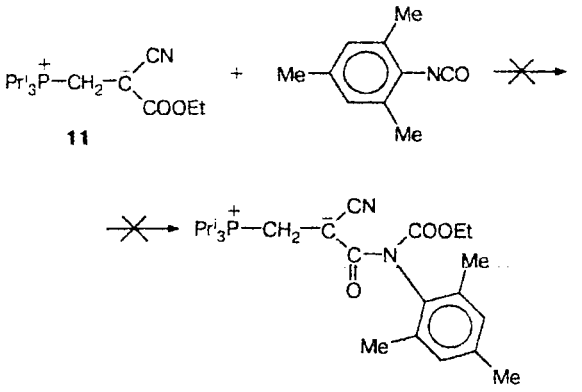
$$\lg k_2 = -(3.049\pm0.510) + (2.469\pm0.450)\sigma^*, \quad (2)$$

$$N = 5,\ r = 0.9950,\ s_0 = 0.022.$$

The rather high positive value of ρ (+2.413), which attests to a high polarity of the transition state, is fully consistent with the proposed reaction mechanism.

It should be noted that zwitterion **11** reacts relatively readily with *meta*- or *para*-substituted aryl isocyanates; however, in the case of *ortho*-substituted aryl isocyanates, only polymerization products are formed* (Scheme 10).

Scheme 10

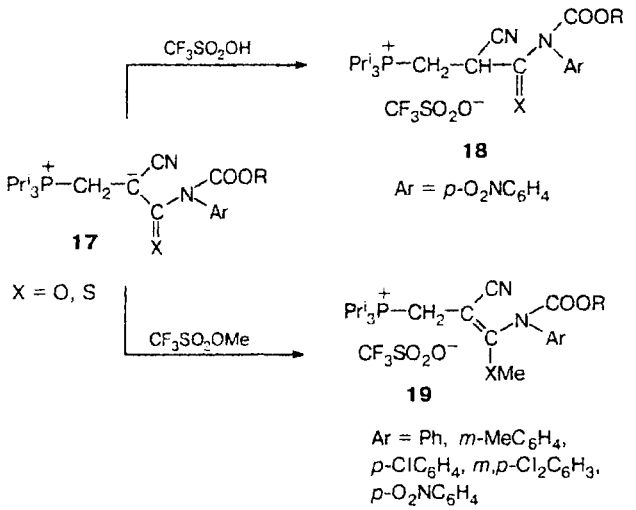


Zwitterions **17** are much less nucleophilic than the initial zwitterion **11**, having a similar structure. Whereas

* Apparently, this is due to steric restrictions in the second step of the process.

the *C*-protonation of these species occurs relatively readily and yields phosphonium salts **18**, their alkylation was attained only on treatment with methyl triflate and gave *O*- or *S*-methylation products **19** (Scheme 11).

Scheme 11

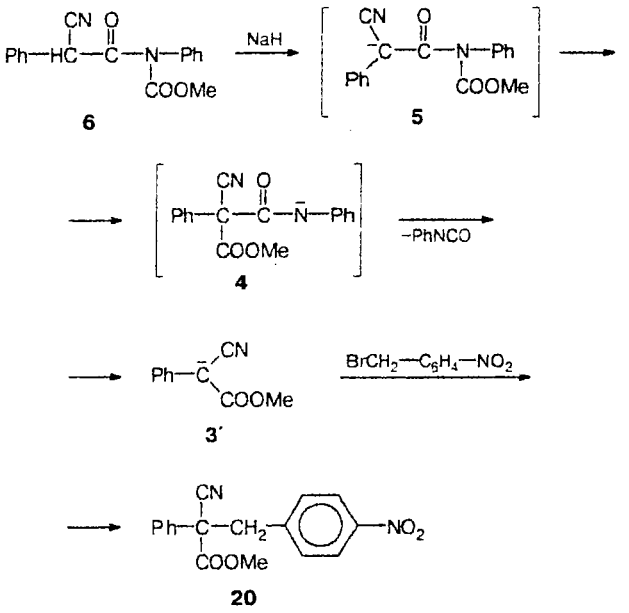


It should be noted that the published data concerning alkylation of α-C-anions derived from *N,N*-dimethylamides[24] indicate that these reactions afford *C*-alkylated derivatives. In our case, the reaction follows the *O*-methylation pattern, obviously, due to the extremely high degree of delocalization of the negative charge in the NCCCO pentad and to the hardness of the methylating reagent. Methylation is strictly stereospecific giving only one geometric isomer with *trans*-arrangement of the phosphonium and carbamate groups. The structure of one methylation product was established by X-ray diffraction analysis.[25]

The C→N rearrangements presented in the general form in Scheme 1 can, in principle, be reversible. This is demonstrated, in particular, by the data concerning the chemical properties of carbamates **6** (more precisely, their conjugated anions **5** and **9**). As noted above (see Scheme 4), the reaction of *p*-nitrobenzyl bromide with the carbanion **5**, arising during the reaction, affords the product of its alkylation **8** in a low yield. However, attempts to alkylate carbanion **5**, formed from CH-acid **6**, by *p*-nitrobenzyl bromide affords the product of alkylation of the carbanion **3'** derived from the initial CH-acid **3**, namely, compound **20**. This can be interpreted only by assuming that back N→C$^-$ migration of the methoxycarbonyl group occurs under the alkylation conditions (Scheme 12).

The back N→C$^-$ migration of the COOMe group occurs in a similar way when bis-carbanion **9** is heated with *p*-nitrobenzyl bromide. In this case, too, ester **20** was isolated from the reaction mixture.

Scheme 12



Studies of other systems suitable for observing C→N$^-$ and N→C$^-$ migrations of electrophilic species are currently in progress; the results obtained will be discussed elsewhere.

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